NHS ENGLAND SPECIALISED SERVICES

CLINICAL PANELREPORT

Date: November 2020

Intervention: Anakinra

Indication: Hemophagocytic lymphohistiocytosis (HLH) (all ages)

URN: 2001

Gateway: 2, Round 1

Programme: Internal Medicine

CRG: Specialised Rheumatology

Information provided to the Panel

Policy Proposition

Evidence review completed by Solutions for Public Health

Equality and Health Inequalities Assessment (EHIA) Report

Clinical Priorities Advisory Group (CPAG) Summary Report

Patient Impact Form

Policy Working Group Appendix

Blueteq® Form

Key elements discussed

This policy proposition recommends the routine commissioning of anakinra for HLH in all ages presenting with primary or secondary HLH regardless of trigger condition, requiring treatment for HLH as part of their clinical care, and in whom first line therapy with corticosteroids has not been effective or would obscure the diagnosis of the underlying condition. Anakinra is needed in the acute phase of HLH for 3-14 days on average and is generally not continued long term.

Clinical Panel was presented with the evidence review including six papers. These comprised of: a comparative cohort study based on a subgroup analysis of adults recruited to an earlier phase III randomised controlled trial; five single centre retrospective case series of paediatric patients. Panel heard that the certainty in the quality of evidence was very low. The key limitation to identifying the effectiveness of anakinra compared to standard treatment for HLH is the lack of reliable comparative studies. They noted that HLH is a rare condition and therefore conducting such studies may be unrealistic. The evidence did report statistically significant evidence that compared to placebo, anakinra reduced 28-day mortality. The number of adverse events reported with anakinra was low.

It was raised that the conclusion of the evidence review was worded negatively given the proposition is recommended for routine commissioning. It was explained that the evidence review is commissioned independently and states the quality and strength of the evidence. The proposition is written by the Policy Working Group. It is the role of Clinical Panel to debate the

evidence base and whether the proposition progresses with the recommended commissioning position or not. This then gets recorded briefly in the committee discussion section of the proposition.

Intravenous immunoglobulin (IVIg) was discussed and the need to reduce usage is important.

Clinical Panel considered the proposition and considered several changes to be made.

The requirement for a multidisciplinary team (MDT) was discussed and funding implications. This requires further exploration. There are a few centres with this expertise although they were thought be easily identifiable.

EHIA considered – no comments received.

Patient Impact Form considered – no comments received.

Recommendation

Clinical Panel recommends that this proposition progresses as a for routine commissioning policy proposition.

Why the panel made these recommendations

The Panel debated the evidence base and there was some concern about the very low certainty in the quality of the evidence and biases in research. However, the Panel considered the rarity of this condition and the impact of this on conducting good quality studies. They considered there was some benefit was demonstrated.

Documentation amendments required

Policy Proposition:

- Inclusion criteria – either remove the point relating to the MDT (c) or incorporate it into one of the other bullet points
- Review the inclusion criteria and that within the Blueteq® form as there is a difference
- Exclusion criteria states those patients who have not had 1st or 2nd line therapies. Policy Working Group to advise on possible earlier use of anakinra
- Medical Advisor for Highly Specialised Services to explore the impact of an MDT and whether this could be funded if recommended in the proposition
- Patient Pathway – use of multiple acronyms which makes it hard to read – Policy Working Group to review

Blueteq® Form:

- Review inclusion criteria against the proposition to align

Declarations of Interest of Panel Members: None

Panel Chair: James Palmer, Medical Director Specialised Services

Post-panel note:

The clinical panel report was discussed with the PWG and the following amendments were made:

- Inclusion criteria – either remove the point relating to the MDT (c) or incorporate it into one of the other bullet points
    - This has been changed and instead it is suggested that management of this rare, complex patient groups should be with the support of an MDT.
- Review the inclusion criteria and that within the Blueteq® form as there is a difference
    - Both the criteria and Blueteq form have been amended, with approval from the Lead Pharmacist
- Exclusion criteria states those patients who have not had 1st or 2nd line therapies. Policy Working Group to advise on possible earlier use of anakinra
    - This has been removed as an exclusion criterion to reflect updated discussions.
- Medical Advisor for Highly Specialised Services to explore the impact of an MDT and whether this could be funded if recommended in the proposition
    - The Medical Advisor for Highly Specialised Services has been informed that the Clinical Lead is aware that there is a well-established, fortnightly virtual MDT run from a London Trust which is accessible across the UK on a case-by-case basis for adult patients. A similar model is being set up in the North of England. MDT costs would be minimal (for minor administrative support). There is also a well-established national paediatric primary HLH MDT. The Medical Advisor for Highly Specialised Services agreed this meets the needs detailed in the proposition.
- Patient Pathway – use of multiple acronyms which makes it hard to read – Policy Working Group to review
    - This has been amended for clarity and an arm to suggest enrolment in random control trials if available has been added.